



NDA 21-015/S-003

Unimed Pharmaceuticals, Inc.
Attention: Judy Athey
Manager, Regulatory Affairs
Four Parkway North
Suite 200
Deerfield, IL 60015-2544

5 SEP 2001

Dear Ms. Athey:

Please refer to your supplemental new drug application dated November 15, 2000, received November 16, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for AndroGel® (testosterone gel).

This "Changes Being Effected" supplemental new drug application provides for the following revisions to the physician package insert that were requested in the August 30, 2000, Supplement Request Letter to furnish adequate information for the safe and effective use of AndroGel®.

DESCRIPTION

“A daily application of AndroGel® 5 G, 7.5 G, or 10 G ~~delivers~~ contains 50 mg, 75 mg, or 100 mg of testosterone, respectively, ~~per day, to be applied daily~~ to the skin’s surface.”

CLINICAL PHARMACOLOGY

Pharmacokinetics

Absorption

....“The skin serves as a reservoir for the sustained release of testosterone into the systemic circulation. Approximately 10% of the testosterone dose applied on the skin surface from AndroGel® is absorbed into systemic circulation. Therefore, 5 G and 10 G of AndroGel® systemically delivers 5 mg and 10 mg of testosterone, respectively. In a study with ~~the~~ 10 G dose of AndroGel® ~~(to deliver 100 mg testosterone)~~, all patients showed an increase in serum testosterone within 30 minutes, and eight of nine patients had a serum testosterone concentration within normal range by 4 hours after the initial application. ...

Figure 1 summarizes the 24-hour pharmacokinetic profiles of testosterone for patients maintained on 5 G or 10 G of AndroGel® ~~(to deliver 50 or 100 mg of testosterone, respectively)~~ for 30 days.”

Clinical Studies

....“During the Initial Treatment Period (Days 1-90), 73 patients were randomized to AndroGel® 5 G daily (to deliver 50 mg testosterone), 78 patients to AndroGel® 10 G daily ~~(to deliver 100 mg testosterone)~~, and 76 patients to a non-scrotal testosterone transdermal system ~~(5 mg daily)~~.

...Patients who were originally randomized to AndroGel® and who had a single-sample serum testosterone levels above or below the normal range on Day 60 were titrated to 7.5 G daily ~~(to deliver 75 mg testosterone)~~ on Day 91.”

DOSAGE AND ADMINISTRATION

“The recommended starting dose of AndroGel® 1% is 5 G ~~(to deliver 50 mg of testosterone)~~ delivering 5 mg of testosterone systemically, applied once daily (preferably in the morning) to clean, dry, intact skin of the upper arms and/or abdomen.”

HOW SUPPLIED

....“AndroGel® is supplied in unit-dose aluminum foil packages in cartons of 30. Each packet of 2.5 G or 5.0 G ~~of gel to deliver 25 mg or 50 mg of testosterone~~, contains 25 mg or 50 mg of testosterone, respectively, and is supplied as follow: ...”

The following editorial revisions were also incorporated:

- changed “TM” to “®”
- replaced “peliosis hepatitis” with “peliosis hepatis” (a typographical error), in the **WARNINGS** section, paragraph 1, sentence 1
- added “A Solvay Pharmaceuticals, Inc. Company” to the address in the **MANUFACTURED BY** section

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert submitted November 15, 2000). Accordingly, the supplemental application is approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Jeanine Best, M.S.N., R.N., Senior Regulatory Associate, at (301) 827-4260.

Sincerely,

Susan Allen, M.D., M.P.H.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research